changed between the two time periods. Also, the use of PBSC instead of BMSC increased (P=0.0001). In order to evaluate the relative importance of these factors a multivariate analysis will be performed. **Conclusion:** The pronounced improvement in TRM during recent years seem to be multi factorial however, an improved donor selection strategy is probably the main cause.

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IMPROVEMENT OF MATCHED SIBLING DONOR ENGRAFTMENT WITH SIROLIMUS ADDED TO A NON-MYELOABLATIVE CONDITIONING REGIMEN

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Non-myeloablative regimens extend the benefit of allogeneic hematopoietic transplantation to many otherwise ineligible patients. Anti-tumor effects are however thought not to occur for most patients until full donor chimerism is achieved. We have recently added sirolimus to an established conditioning regimen in an attempt to optimize engraftment and anti-tumor effects while minimizing morbid GVHD. We compare results of two sequential studies conditioning patients with hematological malignancies with cyclophosphamide (days −7 and −6) and fludarabine (days −7 through −3) prior to matched sibling peripheral blood stem cell transplantation. All received tacrolimus and methotrexate immunoprophylaxis. 9 patients were enrolled in the initial study, and 6/9 also received Campath 1H 20 mg IV on day −7 of the regimen. The second study has treated 10 patients with sirolimus added to the immunosuppression and adjusted to 5–15 ng/ml beginning on day −7 (no Campath was given on this study). Tacrolimus has been tapered off in this protocol between days 30–45, but sirolimus has continued. Graft versus host disease occurred prior to day 100 in 5/9 patients on protocol 1 and 2/10 patients on protocol 2. In all cases GVHD was controllable and no patient has died of transplant related causes. In both protocols all patients showed some degree of donor engraftment by RFLP or XY FISH analysis by day 30. Mean fractional peripheral blood donor chimerism values through day 180 are given in the table below. There is no significant interaction between treatment and time (p-value=0.8579), hence the engraftment curves for the two protocols are parallel. Based on a repeated measures analysis using general F-statistics, there is a significant treatment effect, with patients on the second protocol showing an average of 18% higher engraftment (p-value=0.0281). While follow-up is shorter for patients on Protocol 2, 8/10 patients are beyond 180 days from transplant and the other two have both achieved >0.98 fractional donor engraftment. We conclude that our second protocol, using sirolimus with early tapering of tacrolimus, appears to yield more rapid and complete donor chimerism (Table).

Donor Fractional Whole Blood Chimerism

	Day 15	Day 30	Day 100	Day 180
Protocol 1	**0.51**	**0.75**	**0.82**	**0.81**
Protocol 2 with Sirolimus	**0.72**	**0.88**	**0.99**	**1.00**

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IMATINIB ONLY FOR MOLECULAR RELAPSE IS NOT SUFFICIENT TO ACHIEVE A DURABLE COMPLETE CHIMERIC STATUS AND MOLECULAR REMISSION AFTER ALLO HCT IN CML

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Background: Allogeneic hematopoietic cell transplantation (AlloHCT); today, is still the only treatment modality that provides cure for CML. But relapses after AlloHCT are still an ongoing problem. In most of these patients donor lymphocyte infusions (DLI) are effective to achieve molecular remission (MR). Post DLI aplasia and GVHD are the most important reasons of morbidity and mortality in these patients. Imatinib is a tyrosine kinase inhibitor and blocks CML progenitor cell proliferation. The effect of imatinib on relapse after AlloHCT has been investigated in a few studies including patients with chronic and accelerated phase CML. In this study we aimed to analyze the effect of imatinib on post AlloHCT molecular relapse. **Patients and Method:** Imatinib was applied 400 mg/day p.o. at least for six months to 11 patients; transplanted from their HLA identical siblings with molecular relapse. Patients were monitored closely with ATM Multiplex PCR for chimerism and RQ-PCR (LightCycler, Roche Diagnostics) for bcr-abl/G6PDH. **Results:** Eleven of the patients were under imatinib treatment for more than 6 months. Seven of the 11 patients responded to imatinib. At the end of the sixth month except two patients all of them had donor type chimerism. Periorbital edema developed in 4 of the patients, and none of the patients had Gr 3–4 GIS and hematologic side effect. After cessation of the drug five patients had durable MR and complete chimeric (CC) status. Two patients with second molecular relapse and mix chimeric status after imatinib, and four patients with primary imatinib resistance received DLI. After median 12 (6–20) months follow up, imatinib sensitive 5 patients were in continuing MR, imatinib sensitive two patients with second relapse were in MR and CC after DLI. One of the imatinib refractory patients was lost after DLI induced acute GVHD in MR, The remaining patients did not achieve MR. One patient is still receiving DLI, IFN and imatinib. **Conclusion:** Imatinib treatment for molecular relapse after AlloHCT has acceptable adverse event profile and provides over 60% MR rate but this response was not durable as in DLI; 25% of the patients experience second relapse early after cessation of the drug. DLI may achieve MR in 50% of the primary imatinib resistant patients. Concerning the in vitro effect if imatinib on T cell functions there is an urgent need for prospective studies comparing DLI and imatinib ± DLI with close follow up of chimerism.

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CAN WE CONSIDER FLUDARABINE/ FULL DOSE I.V. BUSULFAN A REDUCED INTENSITY CONDITIONING REGIMEN?

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In this study we analyzed 22 patients who received an allogeneic HSCT from matched related (n=17) or unrelated (n=5) donors, and were conditioned with FLU/BU (fludarabine 30 mg/m^2/d × 4 days followed by single dose i.v. busulfan 3.2 mg/kg/d × 4 days) (n=12) or with the FLU/MEL (fludarabine 30 mg/m^2/d × 5 days and melphalan 70 mg/m^2/d × 2 days) (n=10) RIC regimen. Median age was 26 yrs (range: 19–51) in the FLU/BU group and 47 yrs (range: 22–57) in the FLU/MEL group (p=0.02). High risk patients were 8/12 in the FLU/BU group (7 AML in relapse, 1 CML-AP) and 3/10 in the FLU/MEL group (2 resistant NHL and 1 HD). GVHD prophylaxis was FK-506/MTX and in 9/12 FLU/BU cases (including 5 MUD) Thymoglobulin was added. All FLU/MEL and 6/12 FLU/BU patients received PBSC (median nr. CD34$^+$ cells: 5.0 and 5.9 × 10^6/kg, respectively), while 6 FLU/BU received marrow cells (median nr. CD34$^+$ cells: 1.58 × 10^6/kg). Median time to ANC >500 was comparable in PBSC FLU/BU (d14, range: 11–20), and PBSC FLU/MEL (d12, range: 10–15) patients, while it was longer in bone marrow FLU/BU (d 22, range: 17–37) patients (p= 0.01 and p=0.001, respectively). Time to Plt >20K was d 12 (range: 10–16) in the PBSC FLU/MEL group and d 20 (range: 17–37) in the bone marrow FLU/BUS group. Four of 6 PBSC FLU/BU patients did not have severe thrombocytopenia (<20K) after transplant. Mucositis > grade 2 was never observed. Median length of stay in the hospital after transplant was 17 days (range: 13–37) in PBSC FLU/MEL, 23 days (range: 18–42) in PBSC FLU/BU and 30 d (range: 22–38) in bone marrow FLU/BU. Median chimerism levels on d30 after transplant were: 100% in FLU/MEL and 95% (1 rejection) in FLU/BU. Median follow-up for patients currently alive is 254 days (range: 145–628) in the FLU/BU group and 636 days (range: 429–715) in the FLU/MEL group. Acute GVHD grade II-IV was seen in 1 FLU/BU patient after DLI and in 1 FLU/MEL patient. Chronic GVHD is